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Original article

Misoprostol for induction of second trimester abortion in pregnancies resulting from sexual violence: effectiveness analysis of a protocol applied in the Brazilian public health service☆

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ABSTRACT

Objective: To evaluate the effectiveness of misoprostol protocol on abortion of pregnancies resulting from sexual violence.

Method: Retrospective study with a convenience sample of 253 patients with pregnancy between 13 and 22 weeks of pregnancy who underwent legal abortion in the Hospital Pérola Byington, São Paulo, Brazil, between January 2008 and December 2014. Doses of misoprostol 400 μg (13–17 weeks of gestation) and 200 μg (18–22 weeks of gestation) were administered vaginally every 12 h. The dose was doubled after two doses of no response and maintained for up to four days. In the absence of fetal expulsion, a second cycle of misoprostol was conducted after a 72-h pause. The failure of misoprostol was considered complete after two cycles without fetal elimination. The outcome was complete or incomplete fetal expulsion, evaluated in number of days and misoprostol dose required for abortion. Data were entered in Microsoft Excel 2010 program.

Results: The age ranged from 11 to 44 years of age, average 22.6 ± 8.2 years of age, with the mean gestational age of 16.8 ± 2.6 weeks. Abortion occurred in 248 cases (98.0%) with an average of 1468.8 μg of misoprostol. The analysis of the dispersion of the total dose of misoprostol indicates no significant change with increasing gestational age ($y = 0.9475x + 1453$) ($R^2 = 0.0001$). The average induction time was 2.3 days and in 81.8% of the cases abortion occurred in the first 72 h. Excessive and immediate uterine bleeding after fetal elimination was observed in 2.6% of the cases.

Conclusion: Misoprostol protocol used was effective and safe for second trimester abortion in pregnancy resulting from sexual violence.

☆ Study conducted at the Sexual Violence Center and Legal Abortion, Hospital Pérola Byington, São Paulo, SP, Brazil.

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Misoprostol no aborto de segundo trimestre em gestações decorrentes de violência sexual: análise de efetividade de um protocolo aplicado em serviço público de saúde brasileiro

Palavras-chave:
Aborto legal
Violência sexual
Misoprostol
Aborto induzido
Segundo trimestre de gravidez

RESUMO

Objetivo: Avaliar a efetividade de um protocolo de administração de misoprostol no aborto de gestações decorrentes de violência sexual.

Método: Estudo retrospectivo com amostra de conveniência com 253 pacientes com gestação entre 13 e 22 semanas que fizeram aborto legal no Hospital Pérola Byington, São Paulo, Brasil, entre janeiro de 2008 e dezembro de 2014. Foram administradas doses de misoprostol de 400 microgramas (gestações de 13-17 semanas) e 200 microgramas (gestações de 18-22 semanas), via vaginal, a cada 12 horas. A dose foi duplicada após duas doses sem resposta e mantida por até quatro dias. Na ausência de expulsão fetal, um segundo ciclo de misoprostol foi feito após pausa de 72 horas. A falha do misoprostol foi considerada após dois ciclos completos sem eliminação fetal. O desfecho foi a expulsão fetal, completa ou incompleta, avaliada em número de dias e dose de misoprostol necessária para o aborto. Dados digitados em programa Microsoft Excel® 2010.

Resultados: A idade variou de 11-44 anos, média de 22,6 ± 8,2 anos, com idade gestacional média de 16,8 ± 2,6 semanas. O aborto ocorreu em 248 casos (98%) com média de 1.468,8 microgramas de misoprostol. A análise da dispersão da dose total de misoprostol indica que não houve variação significativa em função do aumento da idade gestacional ($y = 0{,}9475x + 1453$) ($R^2 = 0{,}0001$). O tempo médio de indução foi de 2,3 dias e em 81,8% dos casos o aborto ocorreu nas primeiras 72 horas. Sangramento uterino excessivo e imediato após a eliminação fetal foi observado em 2,6% dos casos.

Conclusão: O protocolo de misoprostol usado se mostrou eficaz e seguro para o aborto de segundo trimestre na gravidez decorrente de violência sexual.

Introduction

Brazilian criminal law criminalizes the practice of abortion, except the situations covered by Article 128 establishing a woman's right to terminate the pregnancy resulting from sexual violence or when there is risk of death for pregnant women.[1] Although Brazilian legislation allows abortion in such circumstances since 1940, only in the late 1980 emerged the first public health services which began to offer legal abortion of first trimester pregnancies.[2]

Since then, there has been slow growth in Brazilian health services committed to human and reproductive rights of women in situations of sexual violence. But despite the improvements, most Brazilian women still lack access to safe and legal abortion in cases of sexual violence, particularly when they are in the second trimester of pregnancy.[2]

Since 1999, the United Nations General Assembly stipulates that in circumstances where abortion is not against the law, health services should be prepared to offer termination of pregnancy safely and at affordable conditions for women.[3] Accordingly, misoprostol is one of the methods of choice for legal interruption of pregnancies between 13 and 22 weeks.

Misoprostol is a methyl-analog synthetic of prostaglandin PGE1, stable at room temperature and effective to promote changes in cervical immature and induce uterine contractility.[4] Prostaglandins are derived from unsaturated monocarboxylic fatty acids of 20 carbons, formed by two chains and the five-carbon ring. The differentiation of the prostaglandins occurs by variations in methylation and oxidation of carbon chains with more or fewer double bonds in the aliphatic side chain.[5]

Misoprostol is known to be effective to induce abortion, although the time required to complete the interruption of pregnancy is greater than when the prostaglandin is associated with mifepristone.[6] Furthermore, abortion is often painful and with more frequent adverse effects than when combined with mifepristona.[7]

In the 1980s, misoprostol started to be used in gynecology and obstetrics after initial indication for treatment of dyspepsia. Compared with other prostaglandins, misoprostol has a lower rate of side effects, with pharmacological extended average life and easier administration by different routes.[8] These features make misoprostol the medication of choice for induction of abortion, cervical preparation and induction of labor.[9]

In Brazil, the Ministry of Health published in 1999, the first misoprostol use protocol for legally induced abortion in pregnancies resulting from sexual violence. A dose of 200 μg was recommended vaginally every 8 h, without defining the time of treatment or management in cases of failure. In 2005, the second edition of the protocol began to indicate doses of 400 μg of misoprostol vaginally every 12 h.[10]

This approach was maintained until 2011, when the Ministry of Health started to recommend different doses according

to gestational age, to the extent that uterine responsiveness to misoprostol increases directly with gestational age.[4] Between 13 and 15 gestation weeks, the recommended dose increased to 400 μg in the vaginal route every 6 to 12 h, and increased to 800 μg after two unsuccessful doses. Between 16 and 22 weeks, the recommended starting dose changed to 200 μg every 6–12 h, and increased to 400 μg doses after two unsuccessful doses.[10]

The Ministry of Health recognizes in its documents the extensive evidence of other protocols in the use of misoprostol for induced abortion presenting with relatively similar rates of success and security for women.[10] Thus, it recognizes that the use of misoprostol should consider the experience gained by the health services.

There is little information of Brazilian health services on the termination of pregnancy resulting from sexual violence. Furthermore, most of these health care services restrict these cases up to 12 weeks of pregnancy. In Brazil, few publications abord the management of second quarter pregnancy with misoprospol under sexual violence circumstance. Thus, the objective is to evaluate the effectiveness of a misoprostol protocol on abortion of pregnancies resulting from sexual violence.

Method

Study design

Descriptive and retrospective study with convenience samples of 253 women with pregnancy resulting from sexual violence, with gestational age between 13 and 22 weeks and who underwent Legal Abortion in Hospital Pérola Byington, São Paulo, Brazil, between January 2008 and December 2014.

Criteria for selection and inclusion of subjects

Adult women and adolescents who sought legal interruption of pregnancy were included based on the item II of Article 128 of the Brazilian Penal Code, which establishes the absence of crime and punishment when abortion is consented and practiced by doctor in pregnancies resulting from sexual crime. Patients with obstetric ultrasound examination with gestational age between 13 and 22 weeks, living fetus and estimated weight less than 500 g were included in this research, according to the World Health Organization definition of abortion.[11]

The characterization of sexual crime has considered the patients' and their legal representatives' reports consistent with Articles 213 and/or 217-A of the Brazilian criminal law. Article 213 criminalizes crime of rape as any sexual act not consented, and practiced with use of physical force and/or serious threat. Article 217-A of vulnerable crime of rape includes sexual acts against children and adolescents younger than 14 years of age, or against those of any age who cannot offer resistance or valid consent.[1] These two items feature the situations of sexual violence, a necessary criterion for the legal termination of pregnancy.

The approval of abortion was the result of the interdisciplinary team consensus upon fulfillment of regulations of the ordinance MH/MG No. 1508, the Ministry of Health, which provide for the supporting procedures and pregnancy termination authorization under the Unified Health System (SUS). It was not required to provide police report or results of forensic examination for the approval of the procedure.[10]

The induction of abortion exclusively used misoprostol and had no association with other physical or medical method according to Hospital Pérola Byington Protocol between the period of January 2008 and December 2014. Initial doses of 400 μg of misoprostol were administered to pregnancies between 13 and 17 weeks and 200 μg in pregnancies between 18 and 22 weeks. The tablets were applied in lateral vaginal fornix every 12 h. The initial dose was doubled to 800 and 400 μg for gestational ages between 13–17 weeks and 18–22 weeks, respectively, after administration of two consecutive doses with no uterine response and fetal deletion, maintained for up to four days.

In cases where there was no fetal expulsion, a second induction cycle with misoprostol was performed after a 72-h pause at doses of 800 and 400 μg for pregnancies between 13–17 weeks and 18–22 weeks, respectively, every 12 h, administered vaginally, for four days. The absence of fetal expulsion after two complete cycles of treatment was adopted as the criterion for induction failure. The possibility of failure by misoprostol was notified to patients prior to initiation of treatment and for such cases abortion was concluded by laparotomy, anterior longitudinal hysterectomy, and fetal placental extract.

Abortion was considered complete when the clinical inspection proved compatible with expulsion of the fetus, placenta, umbilical cord and membranes, accompanied by reduction in uterine volume, progressive closure of the cervix within 24 h and absence of abnormal uterine bleeding.

In suspicion of ovular remains, the ultrasound was made within the first 12 hours. The abortion was considered complete when there was empty uterine cavity and endometrial thickness below 15 mm in longitudinal section. In other cases, the utrasonography was performed seven to ten days after the abortion during follow-up of the procedure.

Instruments

Data were collected from the database organized in Microsoft Excell® 2010. The program database power was accomplished through additional pre-coded card adopted by the hospital. Each case included was previously submitted to review the consistency of information before typing and discrepancies which may be identified were corrected in the complementary record. After entering the data in Microsoft Excel® 2010 spreadsheet, a second review was conducted to identify possible typing errors.

Statistical analysis

The study endpoint was the complete or incomplete fetal expulsion, evaluated in number of days and misoprostol dose required for abortion. Dispersion analysis was employed to evaluate the dose of misoprostol required for fetal delivery as a function of gestational age.

Ethical aspects

The study was approved by the Research Ethics Committee of the Hospital Pérola Byington, Protocol No. 034/11, in September 2011, according to Resolution of the National Health Council (Conselho Nacional de Saúde-CNS) No 196/96. For being a study based on a sample of convenience and consolidated database, it was not necessary to obtain Terms of Consent.

The database used did not include the name, initials, identification, medical record number or any other form of registration that would allow the identification of patients, to ensure the confidentiality and secrecy of information. All women and adolescents received medical, social and psychological counseling, including guidance on ethical and legal issues relating to abortion.

Results

The 253 cases studied corresponded to 38.5% of the total of 657 legal abortions by sexual violence carried out from January 2008 to December 2014. The age of patients ranged from 11 to 44 years, with an average of 22.6 ± 8.25. Teens (10–19 years of age) accounted for 94 cases (37.1%) and adult women (≥20 years) for 159 cases (62.9%). Gestational age ranged between 13 and 22 weeks, 16.8 ± 2.6 media weeks.

The misoprostol was effective in inducing abortion in 248 cases (98.0%) requiring, on average, 1468.8 μg and an average induction time of 2.3 days. The abortion was classified as total in 196 cases (77.5%). The analysis of the dispersion of the total dose of misoprostol required for fetal expulsion showed no significant variation as a function of increasing gestational age ($y = 0.9475x + 1453$) ($R^2 = 0.0001$) (Fig. 1).

The distribution of number of days required for induction termination of pregnancy showed that in 162 cases (61.6%) abortion occurred in the first 48 h (Fig. 2). The accumulated rate in 72 h was 81.8%, equivalent to 207 cases.

Abnormal uterine bleeding, excessive and immediately after fetal elimination, was observed in seven cases (2.6%). In four cases (1.6%) bleeding was controlled with usual measures to promote uterine contractility and complementary evacuation by curettage without need for blood transfusion. In three other cases (1.2%), it was necessary, in addition to previous measures, the use of red blood cells to correct the blood loss, but without further sequelae. No other complications were identified.

Discussion

Sexual violence is a serious violation of human rights and a major public health problem, representing the extreme restriction of sexual and reproductive autonomy of women.[2] Regardless of the legal definition adopted in each country, sexual violence is recognized by the World Health Organization (WHO) as any sexual act, attempted or completed without the consent of the victim, exercised through coercion or intimidation, with use of physical force, threat, weapons or psychological fear.[12]

Although no one knows the exact prevalence of sexual violence, studies point to a worldwide problem of great magnitude and rapid growth.[13] Women who suffer sexual crimes pose a significant hazard to health problems, including physical trauma, mortality, sexual dysfunction, severe psychological damage, sexually transmitted diseases and forced and unwanted pregnancy.[14]

In Brazil, the number of women who resort early to emergency services after sexual crime has increased, although it is acknowledged that most of the victims do not seek for medical care when there are no physical injuries. In three studies, in Brazilian urban centers, between 80% and 95% of women enrolled within 72 h of sexual violence.[15] Quick access to health services allows important intervention measures, such as preventing unwanted pregnancy with the use of emergency contraception.

However, there is evidence that different phenomenon occurs when sexual violence results in pregnancy. Study by Blake et al. identified different factors that can slow the search of Brazilian women for the legal termination of pregnancy. In pregnancies between 13 and 22 weeks, the low education and women's state of vulnerability were associated with this late search. However, victims of violence whose perpetrator was

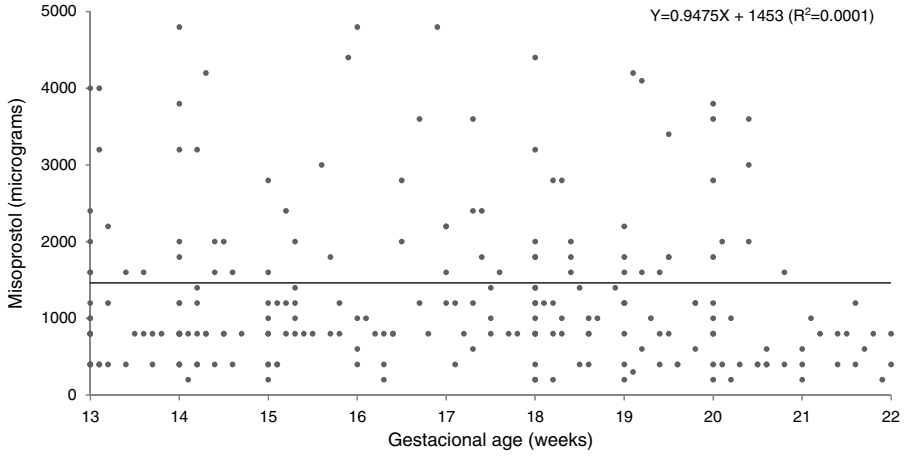

Fig. 1 – Dispersion of the total dose of misoprostol administered to the abortion procedure in relation to gestational age in weeks. Hospital Pérola Byington, São Paulo, Brazil (2008–2014).

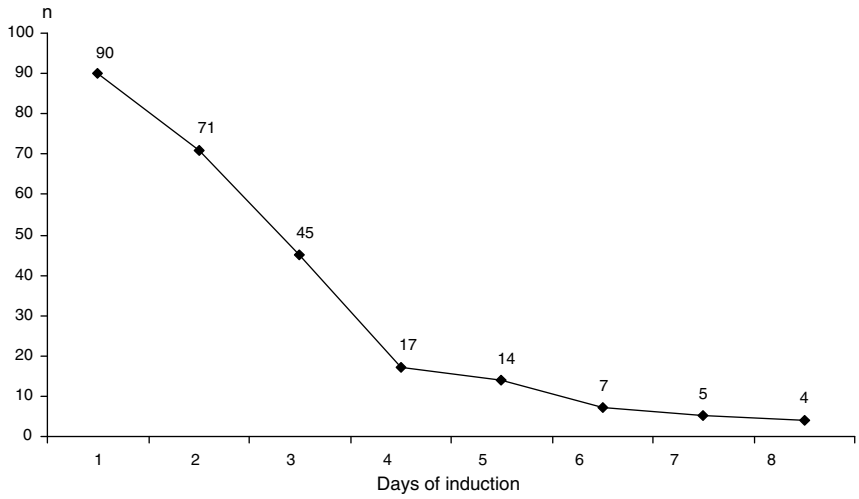

Fig. 2 – Number distribution of 253 misoprostol induced abortions in regard to the number of days required for fetal expulsion. Hospital Pérola Byington, São Paulo, Brazil (2008–2014).

related to them were the ones who found greater barriers to get to health care.[16]

Anyway, due to ignorance of their rights or access barriers to health insurance, many women, convinced in interrupting their pregnancy resulting from sexual violence, resort to illegal abortion procedures often carried out in unsafe conditions.[2]

Since the International Conference on Population and Development in Cairo in 1994, abortion was declared a serious public health problem.[3] In 2003, 20 million unsafe abortions were performed in the world. In 2008, that number increased to 22 million, while the overall abortion rate has not been changed since 2000. Of these unsafe abortions, 98% are practiced in developing countries, resulting in 47,000 maternal deaths and five million women with complications and sequelae.[17]

Complications of unsafe abortion mainly include uterine bleeding, septicemia and peritonitis. Between 20 and 30% of unsafe abortions cause infection, and between 20 and 40% of the cases end in severe pelvic infection.[17] The risk of death associated with unsafe abortion shows variation in different regions. The abortion mortality rate is 460 per 100,000 procedures in Africa in general, and 520 per 100,000 in sub-Saharan region. In Asia it is 160 per 100,000 and in Latin America 30 per 100,000.[17]

On the other hand, induced abortion performed by skilled health professionals and employing appropriate techniques, in an environment with adequate resources, is considered a high security procedure.[17] In the US, the average rate of lethality of the legal termination of pregnancy is 0.7 deaths per 100,000 procedures. In abortion with gestational age less than nine weeks mortality is 0.1 per 100,000 procedures ten times lower than that observed for spontaneous first trimester abortion. In pregnancies between 16 and 20 weeks the rate rises to 3.4 per 100,000, lower than the unsafe abortion.[18]

Misoprostol protocol analyzed in this study is similar to that proposed by the Latin American Federation of Obstetrics and Gynecology Societies (FLASOG) recommending initial vaginal dose of 400 μg for termination of pregnancy between 13 and 15 weeks, and 200 μg between 16 and 20 weeks. These doses are repeated every six to 12 h and doubled after two doses with no success, and maintained at every 12 h up to the maximum of four doses.[4]

The bioavailability of misoprostol when administered by the vaginal route is about three times greater than the oral route. The vaginal route progressively reaches a maximum plasma concentration from 60 to 120 min, followed by a slow decline that reaches 60% of baseline levels after 240 min. The plasma levels remain relatively stable for at least 6 h after the administration.[19] The vaginal route proves more effective than the oral route and results with higher doses of misoprostol orally are similar to those observed with lower doses via vaginal route.[20]

The results of the efficacy of misoprostol studies to induce abortion show great variation, especially by employing different administration schemes. In general, the success rate with complete expulsion of pregnancy is about 90% in both the first and second trimester of pregnancy. If the success criteria is fetal expulsion, even if incomplete, success exceeds 90%.[4] The reduction in the efficacy of misoprostol in the presence of vaginal and cervical infections is still unclear and contradictory data.[21]

In this study, we adopted the criterion of complete or incomplete fetal expulsion, as an indicator of the success of inducing abortion. This explains, in part, the high efficiency of 98% in the termination of pregnancy resulting from sexual crime. Another aspect to be considered is the handling time for up to two cycles, and the use of up to eight doses per cycle, to the extent that there is evidence that better results are obtained by longer waiting time and the days of treatment.[7] However, the results do not seem to be influenced by age, ethnicity, or previous pregnancy.[4]

In this study, the highest percentage of fetal expulsion of the cases occurred in the first 24 h of treatment, with 35.5% of total interruptions. In addition, 81.8% fetal deletion occurred in the first 72 h. These findings agree with the observations of other authors.[7,22–24]

There are few conditions that limit the use of misoprostol, such as severe liver dysfunction, coagulopathy or anticoagulant use, and prior history of allergy to prostaglandins.[25] The adverse effects of misoprostol are not usually severe. Vaginal bleeding and pain in the hypogastrium are present in most cases of uterine contractility result, similar to what occurs in spontaneous abortion.[4] Other effects include nausea, vomiting and diarrhea in 10–30% of inductions.[24,26] These manifestations are more common in high doses, short intervals between doses, and use of oral or sublingual route. Fever can also occur with or without chills.[27]

The complication described as more frequent in induced abortion with misoprostol is excessive vaginal bleeding, generally higher than it occurs in the normal menstruation. However, the bleeding is usually not higher than it occurs in spontaneous abortion.[28] The occurrence of prolonged or heavy bleeding is expected in 1–10% of abortions with misoprostol.[4] In this study abnormal bleeding occurred in 2.6% of the cases within the limits described in other studies.

The failure of the method can also be considered a complication, considering the teratogenicity risk with misoprostol exposure in the first trimester of pregnancy.[4] For the women evaluated in this study the failure of 2%, even being considered low, implies in keeping the pregnancy due to rape and it is not acceptable in these circumstances. In these cases, the termination of pregnancy was done by laparotomy and hysterectomy as recommended by the regulations of the Ministry of Health.[10]

Another exceptional complication with the use of misoprostol, but more serious, is uterine rupture, especially in women with previous cesarean section or previous uterine surgery. However, these conditions are not contraindications to the use of misoprostol in up to 22 weeks abortion. Furthermore, evidence suggests that uterine rupture is related to high doses of misoprostol or its use at shorter intervals than recommended.[29]

It is desirable that the misoprostol dose be individualized for different gestational ages, based on the evidence that the uterine response increases directly with gestational age.[4] This proposition was adopted in the analyzed protocol in this study to induce the second trimester abortion with smaller doses for gestational ages between 18 and 22 weeks.

In this regard, the analysis of the dispersion of the total dose of misoprostol required for abortion showed no significant variation as a function of increasing gestational age ($y = 0.9475x + 1453$) ($R^2 = 0.0001$). For both groups of gestational age similar doses of misoprostol were required, averaging 1468.8 μg. However, the use of lower doses in pregnancies between 18 and 22 weeks may be an important factor to reduce the risk of uterine rupture, usually associated with higher doses of the drug.

Conclusions

The protocol analysis of misoprostol was shown as effective and safe to induce abortion in pregnancies resulting from rape. In most cases it occurred in the first few days of induction for abortion in a complete manner. Abnormal uterine bleeding complication was found in the frequency reported in the literature. These cases were treated with measures to promote contractility and emptying complements without sequelae have been registered.

Conflicts of interest

The authors declare no conflicts of interest.

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